

**Program Number:** 119.4      **Day / Time:** Sunday, Nov. 3, 1:45 PM - 2:00 PM

## **DOPAMINE D2 RECEPTOR UPREGULATION REDUCES COCAINE SELF - ADMINISTRATION**

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Dopamine D2 receptor (DRD2) agonists and antagonists can modulate or disrupt cocaine self-administration (SA) behavior. The DRD2 subtype in particular has been suggested as an important component of the reinforcing effects of cocaine and other drugs. Recently, it was reported that low levels of DRD2 was observed in the brains (NAc) of cocaine addicts (Volkow, 1999). The present study was an extension of our general hypothesis and methods used in two previous projects (Thanos et al 2001). These studies assessed the effects of D2 upregulation (via viral vector containing the rat D2cDNA, injected into the NAc), on alcohol drinking in rats. Rats treated with the D2 gene therapy showed attenuated alcohol preference and intake. Since ethanol and cocaine are believed to similarly involve the same reward pathways, we hypothesized that D2 upregulation in the NAc of cocaine-addicted rats would similarly reduce the amount of drug SA by these same rats. The present study examined cocaine IV SA in male Sprague Dawley rats. Baseline SA was established for 2 weeks before the rats were treated with the D2 vector. A 1-way ANOVA showed a significant decrease in the number of infusions post treatment with the vector ( $p < 0.001$ ). Further analysis revealed that the peak effect was observed at 5 days post treatment ( $p < 0.006$ ). That is, a maximum decrease (59%) in the number of cocaine infusions was seen in rats 5 days post treatment with the D2 vector. These results further support the hypothesis that D2 levels play a role in the abuse of psychostimulants such as cocaine. NIDA (DA06891-06) DOE (DE-AC02-98CH10886).

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